

Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 47 and 48 have been canceled without prejudice and claims 39-44 have been amended.

Formal Drawings

Formal drawings with the correct margins are attached herewith.

Oath/Declaration

According to the Office Action, the oath or declaration is defective, and a new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. In explaining the requirement, the Examiner noted that the oath or declaration is defective "because: non-initialed and non-dated alterations have been made to the oath or declaration." Accordingly, a new declaration, duly signed by Wei-Qiang Gao, is herewith attached.

Priority

(1) The Examiner has concluded that Applicants are entitled only to the priority of US Application No. 09/904,766, filed July 12, 2001, because the subject matter of the present application "is not supported by any of the others because the instant subject matter lacks the necessary support under 35 USC 112, first paragraph. As it will be apparent from the rest of the response, Applicants rely on the gene amplification results (Example 92) to establish substantial and specific asserted utility for the polypeptide PRO269. These results were first disclosed in international application PCT/US00/03565 (P2931R1), filed on February 11, 2000, and published as WO 01/53486 on July 26, 2001 (Pages 138-191 (Example 26), specifically at page 183 and in Table 7, pages 152-163).

(2) The current amendment to the specification to include the indication that the international applications to which the present application claims benefit were published in English under PCT Article 21(2) is believed to overcome the present objection.

(3) The current amendment to the specification to include the status of nonprovisional parent application(s) in the priority claim is believed to overcome the present objection.

IDS

The supplemental IDS in compliance with provisions of 37 CFR 1.97 and 1.98 submitted herewith is believed to overcome the present objection.

Title

The current amendment to the title to read "PRO269 POLYPEPTIDES" is believed to overcome the present objection to the title.

Specification

The specification has been objected to for containing an embedded hyperlink. The foregoing amendment, which deleted all embedded hyperlinks or other forms of browser executable code, is believed to overcome this objection.

35 USC § 101

Claims 39-51 were rejected under 35 U.S.C. 101 "because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility." The Examiner specifically noted that "the instant disclosure fails to clearly establish how one of skill in the art could use the claimed invention in a way that constitutes a credible specific and substantial utility." The Examiner specifically cited

Brenner v. Manson as stating that “Congress intended that no patent be granted on a chemical compound whose sole ‘utility’ consists of its potential role as an object of use-testing.”

The rejection is respectfully traversed.

Utility - Legal Standard

According to the Utility Examination Guidelines (“Utility Guidelines”), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted “specific, substantial, and credible utility” or a “well-established utility.”

Under the Utility Guidelines, a utility is “specific” when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of “substantial utility” defines a “real world” use, and derives from the Supreme Court’s holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that “The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility.” In explaining the “substantial utility” standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase “immediate benefit to the public” or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be “currently available” to the public in order to satisfy the utility requirement. “Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a “substantial” utility.” (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P. 2107 II (B) (1) gives the following instruction to patent examiners: “If the applicant has asserted that the claimed invention is useful for

any particular practical purpose ... and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility.”

Finally, the Utility Guidelines restate the Patent Office’s long established position that any asserted utility has to be “credible.” “Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record ... that is probative of the applicant’s assertions.” (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

Applicants submit that the gene amplification data provided in the present application are sufficient to establish a specific, substantial and credible utility for the PRO269 polypeptide.

Gene amplification is an essential mechanism for oncogene activation. It is well known that gene amplification occurs in most solid tumors, and generally is associated with poor prognosis. As described in Example 92 of the present application, the inventors isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 9 (pages 229-234 of the specification), including primary lung cancers of the type and stage indicated in Table 8 (page 227). As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 222, lines 34-36). Gene amplification was monitored using real-time quantitative TaqMan™ PCR. The gene amplification results are set forth in Table 9. As explained in the passage bridging pages 222 and 223, the results of TaqMan™ PCR are reported in ΔC_t units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification, relative to control, two units correspond to 4-fold, 3 units to 8-fold, etc.

amplification. PRO269 showed approximately 2-3-fold amplification in 8 primary lung tumors.

In assessing the value of these data, the Examiner notes that: "There is no specific information on what type of the normal tissue was used as a control and how many normals there were. A single normal sample is not sufficient for basing relative levels of many other samples." The Examiner has apparently overlooked that, as discussed above, control DNA was pooled from the cells of ten normal healthy individuals (page 222, lines 34-36). Accordingly, the results are not based on a single normal sample. Moreover, while the cited sentence does not specifically state the type of normal tissue, one skilled in the art would understand that, as common in this field, the DNA of the reference samples was collected from white blood cells.

The attached Declaration by Audrey Goddard clearly establishes that the TaqMan™ realtime PCR method described in Example 92 has gained wide recognition for its versatility, sensitivity and accuracy, and is in extensive use for the study of gene amplification. The Declaration also confirms that based upon the gene amplification results set forth in Table 9 one of ordinary skill would find it credible that PRO269 is a diagnostic marker of human lung cancer. It is, of course, true that further research might be needed to develop PRO269 into a diagnostic product. However, the fact that such follow-up tests might be necessary, cannot properly lead to the legal conclusion that PRO269 lacks patentable utility.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. The attached Declaration by Audrey Goddard establishes that the asserted utility is viewed "credible" by one skilled in the art. Indeed, the logic underlying Applicants' assertion that PRO269 is a diagnostic marker of lung cancer cannot be viewed as "seriously flawed," and the facts upon which the assertion is based

are not inconsistent with the logic underlying the assertion. It is always possible that an invention fails on its way of development to a commercial product. Thus, despite recent advances in rational drug design, a large percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

35 USC § 112, First Paragraph/Enablement

Claims 39-51 have been rejected under 35 USC §112, first paragraph because “one skilled in the art clearly would not know how to use the claimed invention.” The Examiner noted that “even were the skilled artisan to consider it more likely than not that the PRO269 polypeptide could be used in any one or more of the asserted utilities, it would still require extensive and undue experimentation of the skilled artisan to actually use the PRO269 polypeptide as disclosed.”

Claims 39-43 and 50-51 were further rejected under 35 USC §112, first paragraph because “the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.” The Examiner noted that “without sufficient guidance, the changes which can be made in the PRO269 polypeptide and still maintain the assayable activities disclosed are unpredictable; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.”

In response to the previous rejection under 35 U.S.C. 101, Applicants have shown that the specification discloses a substantial, specific and credible utility for the PRO269 polypeptide or antibodies against it. This specific utility is now recited in the rejected claims by reciting the requirement that the claimed polypeptides be overexpressed in lung

tumors. It is submitted that one skilled in the art was able to practice the claimed invention at the effective priority date of this application without undue experimentation. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of all pending claims under this section.

35 USC § 112, First Paragraph/Written Description

(1) Claims 39-43 and 50-51 have been rejected for alleged lack of sufficient written description within the full scope of claims. The Examiner noted that “the claims are drawn to polypeptides having at least 80%, 85%, 95%, 90%, 95% or 99% sequence identity with a particular disclosed sequence.” In particular, the Examiner pointed out that the claims “do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.”

The claims now recite the requirement that the polypeptide be overexpressed in lung tumors. Accordingly, it is no longer true that the claims are drawn to a genus of polypeptides that is defined only by sequence identity. The Examiner is, therefore, respectfully requested to reconsider and withdraw the present rejection.

(2) Claims 39-44 and 49-51 were rejected under 35 USC 112, first paragraph “as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.” The Examiner specifically noted that the “Applicant’s provision of these assurances would obviate this objection/rejection.” Accordingly, as the amendments to the specification have incorporated the requisite assurances “that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent,” the Examiner is respectfully requested to reconsider and withdraw the present rejection.

35 USC § 112, Second Paragraph

Claims 39-44, 48 and 50-51 have been rejected under 35 USC § 112, second paragraph as “indefinite.” The Examiner noted that “the recitation of ‘the extracellular domain’ ... ‘lacking its associated signal peptide’ (for example claim 39(d)) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain as signal sequences are cleaved from said domains in the process of secretion from the cell.”

The foregoing amendments to the claims are believed to overcome this rejection.

35 USC § 102(b) or 102(a)

(1) Claims 39-51 were rejected under 35 U.S.C. 102(b), or in the alternative under 35 U.S.C. 102(a) “as being anticipated by Wood et al. (WO 99/14328), see pages 1, 12, 399 56, 72, 83-85, 92-98, 101, 108-112, 126-127, 185-187, Figures 35 and 36), as evidenced by the attached alignment ‘D’.”

The publication date of the Wood et al. reference (WO 99/14328) is March 25, 1999.

As presented above, PCT/US00/03565 (P2931R1), filed on February 11, 2000, duly disclosed the overexpression of PRO269 in lung tumor, now recited in the claims. Accordingly, all claims pending in this application are entitled to the February 11, 2000 priority date, and the cited reference is not available as prior art under either 35 USC 102(b).

Wood et al. is not a valid reference under 35 USC 102(a) either. In *In re Wilder*, the court acknowledged that an application claiming a certain compound could avoid the anticipatory effect of a prior publication specifically naming the same compound by showing that the claimed compound has “properties completely different from those attributed to them by the reference description.” 429 F.2d 447, 451, 166 USPQ 545 (C.C.P.A. 1970). Wood et al. describes the PRO269 polypeptide as a newly identified member of the thrombomodulin family, which therefore may be useful as an

antithrombotic agent. In contrast, the present invention identified PRO269 as a marker of lung cancer. Since the properties of the claimed compounds (PRO269 and variants thereof), which are now recited in the claims, are completely different from those attributed to them by the reference description, under *In re Wilder* Wood et al. does not anticipate the claims pending.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

(2) Claims 39-46 and 49-51 were rejected under 35 U.S.C. 102(b) as being anticipated by Valenzuela et al. (WO 00/11015, see pages 1-2, 115-118, 167-168, 171-176, 183-184, 207-209 and pages 68-70 of the sequence listing), as evidenced by the attached alignment 'E'," The publication date of the Valenzuela et al. reference (WO 00/11015) is March 2, 2000. The rejections based on Valenzuela et al. under 35 U.S.C. 102(b) are believed to be moot as all claims pending in this application, as presented above, are entitled to the February 11, 2000 priority date which pre-dates the Valenzuela et al. reference. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

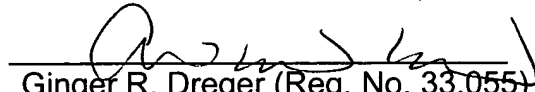
Attached to the present Amendment and Response are sheets marked "**Version with Markings to Show Changes Made**," showing the foregoing claim amendments.

Since all claims pending in this application are believed to be in *prima facie* condition for allowance, an early issuance of a Notice of Allowance is respectfully solicited.

Please charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. 08-1641.

Respectfully submitted,

Date: February 21, 2003


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Version with Markings to Show Changes Made

In the Specification:

The title has been replaced with the following title: --PRO269 POLYPEPTIDES--

The paragraph entered by preliminary amendment August 27, 2002 (Paper No. 10) at page 1, line 2, has been amended as follows:

--This application is a continuation of, and claims priority under 35 USC §120 to, US Application 09/665,350 filed 9/18/2000, which is a continuation of, and claims priority under 35 USC § 120 to, PCT Application PCT/US00/04414 filed 2/22/2000 and published as WO 0 1/04311 on 1/18/01, which is a continuation-in-part of, and claims priority under 3 5 USC § 120 to, PCT Application PCT/US00/03565 filed 2/11/2000 and published as WO 01/53486 on 7/26/01, which is a continuation-in-part of, and claims priority under 35 USC §120 to, PCT Application PCT/US98/19330 filed 9/16/1998 and published as WO 99/14328 on 3/25/99, which claims priority under 35 USC § 119 to US Provisional Application 60/063045 filed 10/24/1997, now abandoned.

The paragraph, beginning at page 69, line 6, has been amended as follows:

--Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). [The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov>.] NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 1515, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.--

The paragraph, beginning at page 71, line 26, has been amended as follows:

--Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). [The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov>.] NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 1515, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.--

The paragraph, beginning at page 147, line 20 has been amended as follows:

--Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, [Rockville, Maryland]Manassas, VA.--

The paragraph beginning at page 147, line 27, has been amended as follows:

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (e.g., Dayhoff, GenBank), and proprietary databases (e.g. LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul, and Gish, Methods in Enzymology 266: 460-80 (1996)[; <http://blast.wustl.edu/blast/README.html>]) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a Blast score of 70 (or in some cases 90) or greater that did not encode known proteins were

clustered and assembled into consensus DNA sequences with the program “phrap” (Phil Green, University of Washington, Seattle, Washington).

The paragraph, beginning at page 154, line 14 has been amended as follows:

--The EST sequence accession number AF007268, a murine fibroblast growth factor (FGF-15) was used to search various public EST databases (e.g., GenBank, Dayhoff, etc.) The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)[; <http://blast.wustl.edu/blast/README.html>]] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. The search resulted in a hit with GenBank EST AA220994, which has been identified as stratagene NT2 neuronal precursor 937230.--

The paragraph beginning at page 167, line 30, has been amended as follows:

--The extracellular domain (ECD) sequences (including the secretion signal, if any) of from about 950 known secreted proteins from the Swiss-Prot public protein database were used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequence. Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program “phrap” (Phil Green, University of Washington, Seattle, Washington[; <http://bozeman.mbt.washington.edu/phrap.docs/Phrap.html>])).

The paragraph beginning at page 178, line 14, has been amended as follows:

--The extracellular domain (ECD) sequences (including the secretion signal, if any) of from about 950 known secreted proteins from the Swiss-Prot public protein database were used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequence. Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington[; <http://bozeman.mbt.washington.edu/phrap.docs/phrap.html>]).--

The paragraph, beginning at page 250, line 2, has been amended as follows:

--The following materials have been deposited with the American Type Culture Collection, [12301 Parklawn Drive, Rockville, MD,]10801 University Boulevard, Manassas, VA USA (ATCC):

<u>Material</u>	<u>ATCC Dep. No.</u>	<u>Deposit Date</u>
DNA32292-1131	ATCC 209258	September 16, 1997
DNA33094-1131	ATCC 209256	September 16, 1997
DNA33223-1136	ATCC 209264	September 16, 1997
DNA34435-1140	ATCC 209250	September 16, 1997
DNA27864-1155	ATCC 209375	October 16, 1997
DNA36350-1158	ATCC 209378	October 16, 1997
DNA32290-1164	ATCC 209384	October 16, 1997
DNA35639-1172	ATCC 209396	October 17, 1997
DNA33092-1202	ATCC 209420	October 28, 1997
DNA49435-1219	ATCC 209480	November 21, 1997
DNA35638-1141	ATCC 209265	September 16, 1997

DNA32298-1132	ATCC 209257	September 16, 1997
DNA33089-1132	ATCC 209262	September 16, 1997
DNA33786-1132	ATCC 209253	September 16, 1997
DNA35918-1174	ATCC 209402	October 17, 1997
DNA37150-1178	ATCC 209401	October 17, 1997
DNA38260-1180	ATCC 209397	October 17, 1997
DNA39969-1185	ATCC 209400	October 17, 1997
DNA32286-1191	ATCC 209385	October 16, 1997
DNA33461-1199	ATCC 209367	October 15, 1997
DNA40628-1216	ATCC 209432	November 7, 1997
DNA33221-1133	ATCC 209263	September 16, 1997
DNA33107-1135	ATCC 209251	September 16, 1997
DNA35557-1137	ATCC 209255	September 16, 1997
DNA34434-1139	ATCC 209252	September 16, 1997
DNA33100-1159	ATCC 209373	October 16, 1997
DNA35600-1162	ATCC 209370	October 16, 1997
DNA34436-1238	ATCC 209523	December 10, 1997
DNA33206-1165	ATCC 209372	October 16, 1997
DNA35558-1167	ATCC 209374	October 16, 1997
DNA35599-1168	ATCC 209373	October 16, 1997
DNA36992-1168	ATCC 209382	October 16, 1997
DNA34407-1169	ATCC 209383	October 16, 1997
DNA35841-1173	ATCC 209403	October 17, 1997
DNA33470-1175	ATCC 209398	October 17, 1997
DNA34431-1177	ATCC 209399	October 17, 1997
DNA39510-1181	ATCC 209392	October 17, 1997
DNA39423-1182	ATCC 209387	October 17, 1997
DNA40620-1183	ATCC 209388	October 17, 1997
DNA40604-1187	ATCC 209394	October 17, 1997
DNA38268-1188	ATCC 209421	October 28, 1997
DNA37151-1193	ATCC 209393	October 17, 1997
DNA35673-1201	ATCC 209418	October 28, 1997
DNA40370-1217	ATCC 209485	November 21, 1997
DNA42551-1217	ATCC 209483	November 21, 1997
DNA39520-1217	ATCC 209482	November 21, 1997
DNA41225-1217	ATCC 209491	November 21, 1997
DNA43318-1217	ATCC 209481	November 21, 1997
DNA40587-1231	ATCC 209438	November 7, 1997
DNA41338-1234	ATCC 209927	June 2, 1998
DNA40981-1234	ATCC 209439	November 7, 1997

DNA37140-1234	ATCC 209489	November 21, 1997
DNA40982-1235	ATCC 209433	November 7, 1997
DNA41379-1236	ATCC 209488	November 21, 1997
DNA44167-1243	ATCC 209434	November 7, 1997
DNA39427-1179	ATCC 209395	October 17, 1997
DNA40603-1232	ATCC 209486	November 21, 1997
DNA43466-1225	ATCC 209490	November 21, 1997
DNA43046-1225	ATCC 209484	November 21, 1997
DNA35668-1171	ATCC 209371	October 16, 1997
DNA77624-2515	ATCC 203553	December 22, 1998--

Please replace the paragraph beginning at page 25 1, line 10, with the following rewritten paragraph:

--These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent, assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC § 122 and the Commissioner's rules pursuant thereto (including 37 CFR § 1.14 with particular reference to 886 OG 638).--

In the Claims:

Claims 47 and 48 have been canceled, without prejudice. Claims 39-44 have been amended as follows:

39. (Once Amended) An isolated polypeptide having at least 80% amino acid sequence identity to:

- (a) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96);
 - (b) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96), lacking its associated signal peptide;
 - (c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96);[
 - (d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96); lacking its associated signal peptide;]
- or

[(e)](d)the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209397, wherein said polypeptide is overexpressed in lung tumors.

40. (Once amended) The isolated polypeptide of Claim 39 having at least 85% amino acid sequence identity to:

- (a) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96);
- (b) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96), lacking its associated signal peptide;
- (c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96);[

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96); lacking its associated signal peptide;]
or

[(e)](d)the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209397, wherein said polypeptide is overexpressed in lung tumors.

41. (Once amended) The isolated polypeptide of Claim 39 having at least 90% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96);

(b) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96), lacking its associated signal peptide;

(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96);[

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96); lacking its associated signal peptide;]
or

[(e)](d)the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209397, wherein said polypeptide is overexpressed in lung tumors.

42. (Once amended) The isolated polypeptide of Claim 39 having at least 95% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96);

(b) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96), lacking its associated signal peptide;

(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96);[

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96); lacking its associated signal peptide;]
or

[(e)](d)the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209397, wherein said polypeptide is overexpressed in lung tumors.

43. (Once amended) The isolated polypeptide of Claim 39 having at least 99% amino acid sequence identity to:

(a) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96);

(b) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96), lacking its associated signal peptide;

(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96);[

(d) the amino acid sequence of the extracellular domain of the polypeptide, shown in Figure 36 (SEQ ID NO:96); lacking its associated signal peptide;]
or

[(e)](d)the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209397, wherein said polypeptide is overexpressed in lung tumors.

44. (Once amended) An isolated polypeptide comprising:

- (a) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96);
- (b) the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO: 96), lacking its associated signal peptide;
- (c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 36 (SEQ ID NO:96);[
- (d) the amino acid sequence of the extracellular domain of the polypeptide, shown in Figure 36 (SEQ ID NO:96); lacking its associated signal peptide;]
- or

[(e)](d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209397, wherein said polypeptide is overexpressed in lung tumors.

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